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Original Article

The Positive Airway Pressure Therapy Compliance in Mild OSAS

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ABSTRACT

Background This study is designed to determine the factors for predicting the PAP compliance in mild obstructive sleep apnea syndrome (OSAS) for improving the cost-effectiveness in the treatment choices of these patients.

Material and Methods The study group comprises 27 mild OSAS patients who underwent automatic positive airway pressure (APAP) titration between July 2016 and December 2017. Demographic, clinic and polysomnographic characteristics of the patients were retrospectively evaluated. Compliance with PAP treatment was defined as the usage of 5 nights/week and 4 hours/night at least. Data of compliant patients were statistically compared with non-compliant patients.

Results Most of the patients (23 patients, 85,2%) were prescribed APAP devices. Acceptable compliance at the end of the first year of therapy was achieved by 11 patients (40,2%) whereas 8 patients used PAP device 2 months at most (29,6%) The remaining 8 patients had not taken the device at all and were considered as non-adherent to PAP treatment (29,6%). The nonadherent/non-compliant group showed statistically the same demographic, clinic, and polysomnographic characteristics when compared to the compliant group. The level of maximum pressure during the titration test was lower in the compliant group (p=0,040).

Conclusions The sleep-related symptoms, scores of Epworth sleepiness scale or polysomnographic parameters can not be used to predict compliance for mild OSAS. The patients with mild OSAS, especially the ones who reach higher maximum pressure on titration test, must be followed up closely during the first 2 months of PAP treatment to detect nonadherence/non-compliance earlier.

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Introduction

Obstructive sleep apnea syndrome (OSAS) is considered mild if the apnea-hypopnea index (AHI) on all-night polysomnography (PSG) is 5-15/hour.[1] Despite the conflicting results about its necessity and efficacy, positive airway pressure (PAP) treatment is proposed as the main choice of treatment in mild OSAS patients with excessive daytime sleepiness, impaired sleep-related quality of life, or cardiovascular comorbidity.[2] This study is designed to determine the factors for predicting the PAP compliance in mild OSAS for improving the cost-effectiveness in the treatment choices of these patients.

Material and Methods

Patient Selection

Out of 3714 patients who underwent PSG in our tertiary hospital sleep center between 01 July 2016 and 31 December 2017, sleep efficiency was not sufficient in 312 patients during the test. Mild OSAS was detected in 493 of the remaining 3402 patients (14.5%). Thirty-six patients with mild OSAS were invited to the titration test due to symptomatic symptoms or accompanying cardiovascular comorbidities. Automatic positive airway pressure (APAP) device could be prescribed for 27 mild OSAS patients who completed the test successfully.

Examining the Data of the Patients Included in the Study

Demographic information (age and gender), disease duration, auto-antibody tests (rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP]) were obtained from records of patients whose

Process

The study group comprises 27 mild OSAS patients who were prescribed PAP treatment after APAP titration with simultaneous PSG between July 2016 and December 2017. Age, gender, body mass index (BMI), symptoms, smoking status, comorbidities and scores on the Epworth Sleepiness Scale (ESS), pulmonary function tests, the results of diagnostic and titration PSG, recordings of PAP device during titration were retrospectively evaluated. Compliance with PAP treatment was defined as the usage of 5 nights/week and 4 hours/night at least. The patients with an ESS score ≥10 were considered to have excessive daytime sleepiness.[3]

The usage profile of the patients was based on either the records of their devices or the statement of the patient. The demographical, clinical, and polysomnographic characteristics of compliant patients were statistically compared with non-compliant patients.

Ethics

The study protocol was approved by the institutional review board of our education and research hospital. The study design was retrospective so ethical committee approval was not required. All procedures performed in this study were held according to the ethical standards of the institutional review board and the 1964 Helsinki declaration and its later amendments. Only the records of patients, who had signed the informed consent for the use of their data, were analyzed.

Measurements

Diagnostic and titration PSGs were performed as full night studies with the digital systems (Neuron-Spectrum EEG and EP neurophysiological system version 1.6.9.6, Neurosoft, Russia and Compumedics Voyager Digital Imaging E-series system Compumedics Ltd, Melbourne, Victoria, Australia) at our sleep laboratory.

For staging sleep four channels of the electroencephalogram, two channels of electrooculogram, one channel of chin electromyogram were used. Respiratory events were scored by using channels of the thermistor, airflow or thoracic and abdominal effort, pulse oximetry, and a microphone for snoring. All records were manually scored according to the criteria of the American Academy of Sleep Medicine (AASM) Scoring Manual Version 2.2[4] by a doctor who has a sleep medicine certificate from the Sleep Society in Turkey.

Different trademarks of APAP devices (ResMed, AutoSet T, Sydney, Australia, Weinman somnobalance, Hamburg, Germany, and Phillips Respironics Remstar Auto Aflex, Murrysville, USA) were used for the titration test. Excessive leak for the nasal mask was defined as the time spent with a large leak is ≥1% for Weinmann

devices, 95th or 90th percentile of nonintentional leakage is ≥24 L/min for Resmed and Phillips devices.

Statistical Analyses

Data analysis was performed using the SPSS software version 15. Descriptive statistics were presented as median (25^{th}-75^{th} percentile). Nominal variables were presented as the number and percentage of cases. Due to the small number of patients in the study group, a non-parametric test (Mann Whitney U test) was performed to compare the distribution of the aforementioned parameters between the groups for numerical data. A Chi-square test was used to examine the difference between groups for categorical variables and p-value <0.05 was accepted as statistically significant.

Results

Out of 28 mild OSAS patients who underwent APAP titration between July 2016 and December 2017, one patient was excluded due to antidepressant treatment. The remaining 27 patients were evaluated. Supine and/or REM predominancy for respiratory events was seen in 81.5% (22 patients) of the patients. Most of the patients (23 patients, 85.2%) were prescribed automated PAP devices. According to the records of the devices and/or oral statement of the patient, acceptable compliance at the end of the first year of therapy was achieved by 11 patients (40.2%) whereas 8 patients used PAP device 2 months at most (29.6%). The remaining 8 patients had not taken the device at all and were considered as non-adherent to PAP treatment (29.6%). As summarized in Table 1,

Table 1. Demographical and clinical characteristics

		All patients median (25.-75.percentile) %(n)	Compliant Median (25.-75.percentile) %(n)	Non-compliant/ Non-adherent Median (25.-75.percentile) %(n)	p value
Age (year)		54 (46-58)	57 (54-67)	51 (57.3-45.3)	0.060
Gender	Female	20 (74.1%)	10 (90.9%)	10 (62.5%)	0.183
	Male	7 (25.9%)	1 (9.1%)	6 (37.5%)	
BMI (n=26)		32.2 (27.8-37.2)	31.7 (28.3-37.5)	33.4 (26.1-37)	0.958
Comorbidities	Total	88.90%	81.80%	93.80%	0.549
Comorbidities	Cardiovascular	74.10%	81.80%	68.80%	0.662
	Metabolic	33.30%	27.30%	37.50%	0.692
	Respiratory	25.90%	36.40%	18.80%	0.391
Smoking status	None smoker	59.10%	62.50%	57.10%	1.000
	Ever-smoked	40.90%	37.50%	42.90%	
PFT (n=26)	FVC (%)	91% (73.8-108.3)	87% (66.3-107.5)	92% (76-111.8)	0.477
	FEV_1 (%)	92% (74.5-108.3)	84% (69.8-99.5)	100.5% (77-110.5)	0.196
	FEV_1/FVC	82.5 (77-86.3)	76.5 (73.8-88)	84 (81.3-85.8)	0.314
ESS		6 (3-7)	6 (2-7)	6 (3.3-10)	0.602
Symptoms	Snoring	92.60%	100%	87.50%	0.499
	EDS	55.60%	54.50%	56.30%	1.000
	Witnessed apnea	74.10%	63.60%	81.30%	0.391

BMI: body mass index, EDS: excessive daytime sleepiness, ESS: Epworth sleepiness scale, FVC: forced vital capacity, FEV_1: forced expiratory volume during the first second, PFT: pulmonary function test.

Table 2. The parameters of diagnostic PSG

		All patients median (25.-75.percentile) %(n)	Compliant Median (25.-75.percentile) %(n)	Non-compliant/ Non-adherent Median (25.-75.percentile) %(n)	p value
TRT (min)		472.2 (453-480.4)	453 (405.5-477.6)	475.5 (464.6-481.5)	0.093
TST (min)		366.5 (390.5-426)	304 (281.5-391.5)	388.5 (346.8-428.3)	0.16
Sleep efficiency (%)		78.2% (70.3-87.8)	72.7 (64.3-85.1)	81.6 (73.3-89.6)	0.256
Sleep latency (min)		12.5 (6-29)	14.5 (8-28)	10.3 (5.1-44.7)	0.639
REM latency (min)		108 (67.5-155.5)	108 (77.5-195)	100 (63-143)	0.199
WASO (min)		57.4 (40.5-102.6)	63.5 (46.7-125.3)	55.6 (38.4-88.5)	0.348
Sleep stages (%)	REM	17.4% (13.3-21.1)	13.8% (9.6-21.1)	19% (15.7-22.1)	0.103
	NREM1	3.5% (1.2-8.9)	5.2% (3.3-15.2)	1.7% (1-7.9)	0.072
	NREM2	56.9% (50.4-64.6)	56.9% (50.4-66.8)	57.3% (50-64.5)	0.961
	NREM3	18.7% (11.2-22)	18.7% (8.4-25.5)	18.9% (12.6-21.8)	0.98
AHI		12.4 (10.9-13.8)	12.4 (11.3-14)	12.5 (10.6-13.7)	0.693
Central AI		0.13 (0-0.21)	0 (0-0.34)	0.14 (0-0.18)	1
Obstructive AI		0 (0-0.98)	0 (0-0.21)	0.09 (0-1.55)	0.329
Hypopnea index		12.1 (9.8-12.9)	12.2 (9.8-13.7)	11.8 (8.6-12.9)	0.554
REM AHI		24.2 (8.7-28.7)	18.1 (4.5-28.2)	25.1 (10.9-28.9)	0.43
Non-REM AHI		9.9 (8.9-11.2)	10.3 (9.3-12.9)	9.8 (8-10.4)	0.132
Supine AHI		14.1 (12.2-20.5)	14.7 (12.7-19.4)	13.6 (11.9-23.4)	0.732
Non-supine AHI		3.2 (0-7.7)	5 (0-8.8)	1.5 (0-6.2)	0.381
Mean SpO_2		91% (90-92)	91% (90-92)	91% (89.3-94.3)	0.881
Minimum SpO_2		81% (75-84)	82% (77-87)	80% (74.3-82.8)	0.216

AHI: apnea-hypopnea index, AI: apnea index, REM: rapid eye movement; TRT: total recording time, TST: total sleep time, WASO: wake after sleep onset.

non-adherent/non-compliant group showed statistically same demographic-clinic characteristics including age, gender, BMI, symptoms, smoking status, comorbidities, and scores on ESS, The high scores of ESS were (ESS ≥11) recorded for only 22% of patients. However, 59.3% of the patients had a complaint of excessive daytime sleepiness (EDS). We could not show any statistically significant difference in the results of PFT, either. The results of diagnostic and titration PSG were also similar for the nonadherent/non-compliant group when compared to the compliant group *(Table 2-3)*. Although statistically insignificant, there were more female patients in the compliant group (p=0.183). As shown in Table 3, the maximum pressure during the titration test was lower in the compliant group (p=0.040). But the differences in an excessive leak, p95, or residue AHI recorded by the device during titration night were not substantial (p>0.05).

Discussion

Previous studies showed that the PAP compliance in mild/moderate OSAS varies between %43-64 for a follow-up lasting 3 weeks-6 months.[5-9] Our study comprised mild OSAS patients solely and we reported the results of a longer follow-up time (1 year). Due to these distinct features of this study, PAP compliance was lower in our study group. Approximately 60% of the patients had not taken the prescribed device or used the device for 2 months at most. This result reflects the accurate rate of compliance for mild OSAS and the importance of the close follow-up during the first two months of the PAP treatment.

In this study, the parameters of PSG including sleep and REM latencies, distribution of sleep stages, and AHI (total, positional, REM AHI, and index for each type of respiratory event),

Table 3. The parameters of titration PSG

		All patients median (25.-75.percentile) %(n)	Compliant Median (25.-75.percentile) %(n)	Non-compliant/ Non-adherent Median (25.-75.percentile) %(n)	p value
TRT (min)		471.4 (456-482.7)	477.4 (456-482.7)	468.3 (453.1-484)	0.459
TST (min)		361 (311-421)	355 (308.9-421)	371.3 (316.2-425.9)	0.844
Sleep efficiency (%)		78.6% (70.6-84)	75.5% (64.6-83.8)	79.8% (71.7-85.8)	0.402
Sleep latency (min)		23.5 (12.5-40.5)	25 (23.5-42.5)	16.3 (6.1-37)	0.109
	REM	16.3% (10.5-21)	14.4% (9.6-18.5)	16.9% (13.7-21.1)	0.348
	NREM1	1.4% (1-2.2)	1.3% (1.1-1.8)	1.5% (0.9-2.5)	0.711
Sleep stages (%)	NREM2	57.1% (52.4-64.7)	55.8% (52.4-68.8)	57.6% (63.8-52.2)	0.921
	NREM3	24.6% (17.3-29.3)	28.1% (23.3-30.3)	23.2% (14-27.9)	0.109
AHI		2.6 (1-3.9)	2.2 (0.9-4.6)	2.7 (1.3-3.9)	0.921
Central AI		0.4 (0-1.4)	0.4 (0-0.9)	0.8 (0.13-1.4)	0.383
Obstructive AHI		1.9 (0.6-3)	0.9 (0.6-3)	2 (0.4-2.8)	0.941
REM AHI		2.4 (0.8-9.2)	1.6 (0.8-4.9)	5 (0.2-9.4)	0.457
Non-REM AHI		2 (0.9-3.3)	2.2 (0.9-3.5)	1.9 (0.9-3)	0.57
Mean SpO_2		93% (91-94)	93% (92-94)	92.5% (90.3-93.8)	0.38
Minimum SpO_2		89% (84-90)	89% (82.90)	89.5% (84.3-90)	0.669
	RDI	(n=27) 1.9 (0.8-4)	(n=11) 1.6 (0.5-3.2)	(n=16) 2.2 (0.9-6.4)	0.256
	p95 (cmH_2O)	(n=23) 8.6 (7-11)	(n=9) 7.7 (6-11.7)	(n=14) 8.8 (7.5-10.6)	0.507
The recordings of PAP devices	Maximum presure (cmH_2O)	(n=23) 9.3 (7.3-11.6)	(n=10) 7.5 (6.9-10.2)	(n=13) 9.8 (8.6-11.8)	0.04
	Excessive mask leak	(n=27)	(n=11)	(n=16)	
	+	59.30%	54.50%	62.50%	0.71
	-	40.70%	45.50%	37.50%	

AHI: apnea-hypopnea index, AI: apnea index, REM: rapid eye movement, TRT: total recording time, TST: total sleep time, RDI: respiratory disturbance index.

wake after sleep onset time, minimum and mean oxygen saturations were also analyzed. But the compliant group did not show any statistical difference in means of these parameters either on diagnostic PSG or PSG during titration. We can conclude that PSG parameters can not be used for predicting compliance for patients with mild OSAS.

Despite the high rates of compliance in symptomatic patients with moderate/severe OSAS[10], our results also noted that sleep-related symptoms or scores of ESS can not be used for estimating the compliance for mild OSAS, either. Nevertheless, we showed that the level of maximum pressure during the titration test was the only parameter statistically promising for the estimation of the treatment compliance for mild OSAS.

The data from the Sleep Heart Health Study demonstrated that 28% of the patients with mild OSAS were sleepy and the quality of life was low.[11,12] The results from the Wisconsin Sleep Cohort Study revealed that the high level of sleepiness also affected the daily activities of snorers with AHI <5 when compared with non-snoring controls.[13] These two population studies also provided evidence for the significant effect of mild OSAS on blood pressure.[14,15] Peppard *et al.*[14] declared that the odds ratio for the 4-year incidence of developing hypertension was 2.03 (1.29-3.17) for AHI between 5 and 14.9. Although the incident risk for adverse

cardiovascular outcomes is unknown, the previous studies pointed out a link between mild OSAS and cardiovascular outcomes.[16,17] It is also known that the risk for endothelial dysfunction, atherosclerosis, and insülin resistance also starts with the mildest degree of OSAS.[18-20]

The outcomes of mild OSAS can be severe in means of cardiovascular and metabolic diseases. The characteristics of this group of patients with mild OSAS and cardiovascular and metabolic diseases must be clarified for selecting the patients who can benefit from the PAP treatment. The last guideline of AASM recommends PAP treatment for OSAS in adults with excessive sleepiness regardless of the severity. A lower degree of recommendation is also proposed for all OSAS patients with the impaired sleep-related quality of life and hypertension.[2] The previous studies published conflicting results for the benefits of APAP on cardiovascular risk, quality of life, and mortality in mild OSAS.[21] Some authors suggest that medical or conservative treatments including weight loss, positional therapy, or nasal corticosteroids may be more effective than PAP treatment in mild OSAS.[22] Additionally, even if the symptoms improve, the patients with mild OSAS are likely to abandon the PAP treatment.[23]

The sympathetic nervous system activation and hypoxia due to apnea/hypopnea and the oxidative stress due to reoxygenation are the main causes of cardiovascular and metabolic events for OSAS.[24]

Eventually, patients with mild OSAS tend for increased cardiovascular events and PAP treatment may lead to an increase in quality of life for a group of patients with mild OSAS.[16-25] We recommend that mild OSAS patients especially those who reach higher maximum pressure on titration test must be followed up closely during the first 2 months of PAP therapy to detect nonadherence and non-compliance earlier.

Our study has some limitations. First, the number of patients is small. The number of patients included in the previous studies range between 29-66 however the studies also include the patients with moderate OSAS.[5-9] Second, the adherence of 40.2% of patients in our study group was based on subjective data from patients' statements. Eventually as there is no benefit in making false statements, we found it trustable.

Conclusion

The number of patients diagnosed with mild OSAS requiring PAP treatment is quite less than moderate/severe OSAS. In the literature, mild OSAS is evaluated together with moderate OSAS. Uniquely, our study investigates mild OSAS solely and has a relatively long follow-up period of 1 year. Therefore, the results of this study will have a significant meaning for the clinicians dealing with sleep disorders.

The risk of complications increases if individuals with symptomatic mild OSAS patients with comorbidities are left untreated. However, parameters predicting poor compliance are needed for a better cost-effective approach, Our results show that the patients who require higher pressure during the titration test can be evaluated as the candidates of poor compliance/ adherence to PAP therapy.

Conflict of Interest

Authors have no conflict of interest to declare.

Authors' Contribution

Study Conception: SSD, DC, FA, SF; Study Design: SSD, DC, FA, SF; Supervision: SSD, DC, FA, SF; Data Collection and/or Processing: SSD, DC; Statistical Analysis and/or Data Interpretation: SSD, DC, FA, SF; Literature Review: SSD, DC; Manuscript Preparation: SSD, DC; Critical Review: SF.

References

1. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep. 1999 Aug 1;22(5):667-89.
2. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of Adult Obstructive Sleep Apnea with Positive Airway Pressure: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med. 2019 Feb 15;15(2):335-43. doi: 10.5664/jcsm.7640.
3. Izci B, Ardic S, Firat H, Sahin A, Altinors M, Karacan I. Reliability and validity studies of the Turkish version of the Epworth Sleepiness Scale. Sleep Breath. 2008 May;12(2):161-8. doi: 10.1007/s11325-007-0145-7.
4. Berry RB, Brooks R, Gamaldo CE, Harding SM, Lloyd RM, Marcus CL, Vaughn BV. The American Academy of Sleep Medicine. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology

and Technical Specifications. 2015. Version 2.3. Darien, Illinois: American Academy of Sleep Medicine.
5. Marshall NS, Neill AM, Campbell AJ, Sheppard DS. Randomised controlled crossover trial of humidified continuous positive airway pressure in mild obstructive sleep apnoea. Thorax. 2005 May;60(5):427-32. doi: 10.1136/thx.2004.032078.
6. Barnes M, McEvoy RD, Banks S, Tarquinio N, Murray CG, Vowles N, Pierce RJ. Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. Am J Respir Crit Care Med. 2004 Sep 15;170(6):656-64. doi: 10.1164/rccm.200311-1571OC.
7. Barnes M, Houston D, Worsnop CJ, Neill AM, Mykytyn IJ, Kay A, Trinder J, Saunders NA, Douglas McEvoy R, Pierce RJ. A randomized controlled trial of continuous positive airway pressure in mild obstructive sleep apnea. Am J Respir Crit Care Med. 2002 Mar 15;165(6):773-80. doi: 10.1164/ajrccm.165.6.2003166.
8. Engleman HM, McDonald JP, Graham D, Lello GE, Kingshott RN, Coleman EL, Mackay TW, Douglas NJ. Randomized crossover trial of two treatments for sleep apnea/hypopnea syndrome: continuous positive airway pressure and mandibular repositioning splint. Am J Respir Crit Care Med. 2002 Sep 15;166(6):855-9. doi: 10.1164/rccm.2109023.
9. Monasterio C, Vidal S, Duran J, Ferrer M, Carmona C, Barbé F, Mayos M, Gonzalez-Mangado N, Juncadella M, Navarro A, Barreira R, Capote F, Mayoralas LR, Peces-Barba G, Alonso J, Montserrat JM. Effectiveness of continuous positive airway pressure in mild sleep apnea-hypopnea syndrome. Am J Respir Crit Care Med. 2001 Sep 15;164(6):939-43. doi: 10.1164/ajrccm.164.6.2008010.
10. Qaseem A, Holty JE, Owens DK, Dallas P, Starkey M, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Management of obstructive sleep apnea in adults: A clinical practice guideline from the American College of Physicians. Ann Intern Med. 2013 Oct 1;159(7):471-83. doi: 10.7326/0003-4819-159-7-201310010-00704.
11. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991 Dec;14(6):540-5. doi: 10.1093/sleep/14.6.540.
12. Baldwin CM, Griffith KA, Nieto FJ, O'Connor GT, Walsleben JA, Redline S. The association of sleep-disordered breathing and sleep symptoms with quality of life in the Sleep Heart Health Study. Sleep. 2001 Feb 1;24(1):96-105. doi: 10.1093/sleep/24.1.96.
13. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med. 1993 Apr 29;328(17):1230-5. doi: 10.1056/NEJM199304293281704.
14. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med. 2000 May 11;342(19):1378-84.doi:10.1056/NEJM200005113421901.
15. Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, D'Agostino RB, Newman AB, Lebowitz MD, Pickering TG. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA. 2000 Apr 12;283(14):1829-36. doi: 10.1001/jama.283.14.1829. Erratum in: JAMA 2002 Oct 23-30;288(16):1985.
16. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Nieto FJ, O'Connor GT, Boland LL, Schwartz JE, Samet JM. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med. 2001 Jan;163(1):19-25. doi: 10.1164/ajrccm.163.1.2001008.
17. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005 Mar 19-25;365(9464):1046-53. doi: 10.1016/S0140-6736(05)71141-7.
18. Reichmuth KJ, Austin D, Skatrud JB, Young T. Association of sleep apnea and type II diabetes: a population-based study. Am J Respir Crit Care Med. 2005 Dec 15;172(12):1590-5. doi: 10.1164/rccm.200504-637OC.
19. Drager LF, Bortolotto LA, Lorenzi MC, Figueiredo AC, Krieger EM, Lorenzi-Filho G. Early signs of atherosclerosis in obstructive sleep apnea. Am J Respir Crit Care Med. 2005 Sep 1;172(5):613-8. doi: 10.1164/rccm.200503-340OC.
20. Duchna HW, Stoohs R, Guilleminault C, Christine Anspach M, Schultze-Werninghaus G, Orth M. Vascular endothelial dysfunction in patients with mild obstructive sleep apnea syndrome. Wien Med Wochenschr. 2006 Nov;156(21-22):596-604. doi: 10.1007/s10354-006-0341-2.
21. Littner MR. Mild obstructive sleep apnea syndrome should not be treated. Con. J Clin Sleep Med. 2007 Apr 15;3(3):263-4.
22. Morgenthaler TI, Kapen S, Lee-Chiong T, Alessi C, Boehlecke B, Brown T, Coleman J, Friedman L, Kapur V, Owens J, Pancer J, Swick T; Standards of Practice Committee; American Academy of Sleep Medicine. Practice parameters for the medical therapy of obstructive sleep apnea. Sleep. 2006 Aug;29(8):1031-5.
23. Whitelaw WA, Brant RF, Flemons WW. Clinical usefulness of home oximetry compared with polysomnography for assessment of sleep apnea. Am J Respir Crit Care Med. 2005 Jan 15;171(2):188-93. doi: 10.1164/rccm.200310-1360OC.
24. Sağmen SB, Parmaksız ET, Cömert SŞ, Fidan A, Salepçi B. Liver functions in patients with obstructive sleep apnea syndrome. The European Research Journal. 2018;4(4):349-55. doi: 10.18621/eurj.381906.
25. Engleman HM, Martin SE, Deary IJ, Douglas NJ. Effect of CPAP therapy on daytime function in patients with mild sleep apnoea/hypopnoea syndrome. Thorax. 1997 Feb;52(2):114-9. doi: 10.1136/thx.52.2.114.